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Clinical Outcomes Following ST-Elevation Myocardial Infarction Secondary to Stent Thrombosis Treated by Percutaneous Coronary Intervention

Short Title: Outcomes of Stent Thrombosis in Myocardial Infarction

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Key Words: Stent Thrombosis, Myocardial Infarction, De Novo Lesions
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Key Words

CAD - Coronary Artery Disease

COMI - Complications, PCI

REST - Restenosis

Abbreviation list

PCI – Percutaneous Coronary Intervention

ST - Stent Thrombosis

STEMI - ST-Elevation Myocardial Infarction

ACS – Acute Coronary Syndrome

MACE – Major Adverse Cardiac Outcomes

MI – Myocardial Infarction

TVR – Target Vessel Revascularization

EST - Early Stent Thrombosis

LST - Late Stent Thrombosis

VLST - Very-Late Stent Thrombosis

STDT - Symptom-To-Door Time

DTBT - Door-To-Balloon Time

STBT - Symptom-To-Balloon Time

Abstract

Objectives: To assess the clinical outcomes of patients presenting with ST-elevation myocardial infarction (STEMI) secondary to stent thrombosis (ST) compared to those presenting with STEMI secondary to a *de novo* culprit lesion and treated by percutaneous coronary intervention (PCI).

Background: ST is an infrequent but serious complication of PCI with substantial associated morbidity and mortality, however with limited data.

Methods: We studied consecutive patients who underwent PCI for STEMI from 2005 to 2013 enrolled prospectively in the Melbourne Interventional Group registry. Patients were divided into two groups, the ST group comprised patients where the STEMI was due to stent thrombosis; the *de novo* group formed the remainder of the STEMI cohort and all patients were treated by PCI. The primary endpoint was 30-day all-cause mortality.

Results: Compared to the *de novo* group (n=3,835), the ST group (n=128; 3.2% of STEMI) had higher rates of diabetes, hypertension and dyslipidemia, established cardiovascular diseases, myocardial infarction and peripheral vascular disease, all $p<0.01$. Within the ST group, very-late ST was the most common form of ST, followed by late and early ST (64%, 19% and 17% respectively). There was no significant difference in the primary outcome

between the ST group and the *de novo* group (4.7% vs. 7.1%, p=0.29). On multivariate analysis, ST was not an independent predictor of 30-day mortality (OR 0.62, 95% CI 0.07-1.09, P=0.068).

Conclusion: The short-term prognosis of patients with STEMI secondary to ST who were treated by PCI was comparable to due to *de novo* lesions.

Introduction

Percutaneous coronary intervention (PCI) is the preferred method for managing ST-elevation myocardial infarction (STEMI) [1,2]. Stent thrombosis (ST) is an uncommon, but recognised complication of PCI with previously described substantial associated morbidity and mortality [3]. The majority of cases of ST present as STEMI [4] with associated lower procedural success rates rendering their management challenging [5]. The use of PCI techniques such as high-pressure stent implantation, high-pressure post-dilation, intra-vascular imaging to achieve optimal stent expansion and apposition, dual anti-platelet therapy in conjunction with improved stent profiles are thought to reduce the frequency of ST in the modern era [6]. Data regarding the outcomes of STEMI secondary to ST as compared to those due to a *de novo* lesion remain sparse with relatively small numbers [7], which limit the assessment of this group of patients. Additionally, the reported high mortality associated with ST appears to be predominantly driven by in-hospital outcomes with very few studies assessing the impact on survival following

discharge from hospital [5]. The aim of this study was to assess the clinical and procedural characteristics as well as the short-term clinical outcomes of patients who underwent PCI for STEMI secondary to ST compared with those who underwent PCI for STEMI related to a *de novo* lesion, using data from a large multi-centre Australian PCI registry.

Methods

This study included prospectively collected data from consecutive patients who underwent PCI for STEMI from 2005 to 2013, enrolled prospectively in the Melbourne Interventional Group (MIG) registry. The MIG registry is a multi-centre PCI registry and has been previously described in detail [8]. Briefly, demographic, clinical, procedural and in-hospital outcome data are prospectively recorded on case-report forms using standardised definitions for all fields with telephone follow up and record review performed at 30 days [9].

The registry is coordinated by the Centre of Cardiovascular Research and Education in Therapeutics; an independent research body within the School of Public Health and Preventive Medicine at Monash University (Melbourne, Australia). An audit of a number of verifiable fields from 5% of randomly selected procedures at each institution is undertaken periodically [9,10]. In the most recent audit, 27 fields were assessed with data accuracy of 98%. This compares favourably to audits from other large registries [11]. The ethics committee in each participating hospital approved the MIG registry, including the use of "opt-out" consent. To "opt-out" means, the participant can choose to have any or all the information about them removed from the MIG registry.

Patients were divided into two groups: (i) the ST group comprised patients with STEMI due to stent thrombosis (see definitions below); (ii) the *de novo* group comprised the remainder of the STEMI population. Baseline demographic, clinical and procedural characteristics, as well as short- and intermediate-term clinical outcomes were compared between the two groups. The primary endpoint was all-cause 30-day mortality.

Secondary endpoints included major adverse cardiovascular events (MACE; a composite of all-cause mortality, myocardial infarction [MI] and target vessel revascularization [TVR]) in-hospital, at 30-day and 12-month follow up, 12-month mortality, and complications such as

major bleeding, stroke and TVR during the index admission, at 30-day and 12-month follow up.

We used the standard definitions of ST as per the Academic Research Consortium and defined ST as the presence of a thrombus or angiographic documentation of vessel occlusion within a pre-existing stent or within 5 mm of the proximal or distal stent edges[12]. We only included definite and probable stent thromboses in the ST-patient group to maximize specificity without compromising sensitivity and to avoid over-reporting of stent thrombotic events. Definite ST was defined as the presence of an acute coronary syndrome (ACS) with angiographic or autopsy evidence of thrombus or occlusion. Probable ST included unexplained deaths during the index admission after the PCI procedure or acute MI involving the target coronary vessel territory without angiographic or autopsy confirmation. Possible ST was excluded from the stent thrombosis patient group and was defined as all unexplained deaths occurring at least 30 days after the procedure. Temporal classifications of stent thrombosis included early stent thrombosis (EST) (0 to 30 days), late stent thrombosis (LST) (31 to 365 days), or very-late stent thrombosis (VLST) (>365 days).

Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range, and categorical variables were expressed as numbers (percentages), except where indicated. Continuous variables were compared using Student's *t*-tests or Kruskal-Wallis equality-of-populations rank test as appropriate. Categorical variables were compared using Pearson's chi-square or Fisher's exact tests as appropriate. All calculated p-values were two-sided and p-values <0.05 were considered statistically significant. Cumulative incidence of all-cause mortality was estimated by the Kaplan-Meier method, and the log-rank test was used to evaluate differences between groups. Cox proportional hazards modelling was used to identify univariate and multivariate predictors of 30-day mortality and 30-day

MACE. Univariate variables with a p-value <0.10 were then included in multivariate models using stepwise backward selection. All statistical analyses were performed using Stata v14.1 for Windows (College Station, TX, USA).

Results

Of 3,963 studied STEMI cases, 128 (3.2%) were secondary to ST and 3,835 (96.8%) related to *de novo* lesions. A comparison of baseline demographic and clinical characteristics between the two groups is presented in Table 1. Patients in the ST group were older and had higher rates of cardiovascular disease risk factors including diabetes mellitus, hypertension, dyslipidemia, and a higher proportion of ex-smokers compared to the *de novo* group (all $p<0.05$). However, the *de novo* group had higher body-mass index and included more current smokers (all $p<0.05$). Established cardiovascular diseases such as previous MI, previous coronary artery bypass graft surgery, heart failure and peripheral vascular disease were more prevalent in the ST group (all $p<0.01$). Compared to the ST group, the *de novo* group had greater rates of out-of-hospital cardiac arrest (OHCA) presentations (11.5% vs. 4.7%, $p=0.017$).

Table 2 demonstrates the procedural findings and characteristics. The ST group had a shorter median symptom-to-door time (STDT) compared to the *de novo* group (102 min [71-162] vs. 114 min [75-210], $p=0.032$). Although there was no difference in the median door-to-balloon time (DTBT) (66 min [43.5-97.5] vs. 67 min [44-96], $p=0.95$) between the two groups, the ST group had a slightly shorter median symptom-to-balloon time (STBT) (185 min [132-239] vs. 194 min [141-291], $p=0.051$). The ST group were more likely to receive treatment with glycoprotein (GP) IIb/IIIa inhibitors and bivalirudin, and less heparin during the procedure compared to the *de novo* group (all $p<0.05$). Within the ST group, VLST was the most common form of ST, followed by LST and EST (64%, 19% and 17% respectively), with a median of 1187 days [119 – 2491] from the procedure to ST.

There were higher rates of LAD-related culprit lesions, complex lesions with a greater severity of stenosis pre- and post-procedure and lower Thrombolysis In Myocardial Infarction

(TIMI) flow grade at the onset of procedure in the ST group (all p<0.05). Overall, procedural success rates were similar between the two groups (94.9% vs. 95.4%, p=0.79) and there were no remarkable differences in procedural complication rates or post-procedural TIMI flow grades. The ST group had greater use of intra-vascular ultrasound (IVUS) and balloon angioplasty with lower rates of stent use (all p<0.001) compared to the *de novo* group. Medication prescription is presented in Table 3 and demonstrates no significant differences between the two groups.

The short- and intermediate-term clinical outcomes are demonstrated in Table 4. There was no significant difference in the primary outcome of 30-day mortality between the ST group and the *de novo* group (4.7% vs. 7.1%, p=0.29). Also, there was no difference in in-hospital mortality, MACE during in-hospital and at 30-day follow up between the two groups (all p>0.05). Figure 1 demonstrates the Kaplan-Meier survival analysis for 30-day mortality and MACE of the two groups. While outcomes were similar between the two groups, in-hospital complications of bleeding and blood transfusion requirements were higher in the ST group (both p<0.01). There was a trend towards higher readmission rates at 30 days in the *de novo* group (7.5% vs. 13.0%, p=0.077).

On multivariate analysis, ST was not independently associated with 30-day mortality (OR 0.62, 95% CI 0.07-1.09, P=0.068) or 30-day MACE (OR 0.88, 95% CI 0.41-1.8, p=0.75), see Table 5 (which shows the multivariate predictors of 30-day mortality and MACE). Within the ST group, stent implantation between 31-365 days prior and that beyond 365 days were also found to lack independent association with 30-day MACE (OR 1.1, 95% CI 0.09-14.4, p=0.89 and OR 0.5, 95% CI 0.06-4.1, p=0.53 respectively).

Discussion

The main findings of this study of a large, long- established multi-centre Australian registry are that patients presenting with STEMI secondary to ST are not at increased risk of in-hospital and 30-day mortality compared to patients with STEMI caused by *de novo* lesions in the modern era of PCI and adjunctive pharmacotherapy. This similarity in outcomes is evident despite demonstrating an older population with higher prevalence of comorbidities such as diabetes, hypertension and dyslipidemia as well as greater prevalence of established cardiac and vascular diseases in the ST group. Compared to the *de novo* group, patients in the ST group presented to hospital earlier, received additional intravenous anti-platelet agents, underwent PCI procedures with higher use of IVUS and balloon angioplasty and endured higher rates of in-hospital bleeding complications. After multivariate adjustments for differences in baseline and procedural characteristics, ST was not an independent predictor of mortality or MACE at 30-day follow up.

The outcomes of ACS secondary to ST compared to *de novo* lesions have been previously described in literature [5,13,14]. Several factors could explain the absence of significant difference of mortality between the two groups. The ST group presented to hospital earlier than the *de novo* group as reflected in the shorter median STDT and STBT. This difference in reperfusion times could have imparted a favourable outcome gain on patients in the ST group. Previous studies had demonstrated worse outcomes associated with longer STBT including mortality in ACS [15-17]. In addition, the earlier presentation to hospital could possibly be related to the heightened perception and early recognition of symptoms of MI, particularly that the majority of the ST group patients have had previous MI compared to the *de novo* group (82% vs. 9%, $p<0.001$). Patients in the ST group presented with lower rates of OHCA compared to the *de novo* group. A possible explanation for these lower rates of OHCA is the pre-hospital

mortality of OHCA patients. We also found no difference in the rates of cardiogenic shock, intra-aortic balloon pump and inotropes utilization between the two groups. This finding is in contrast to other studies [5,7] that reported higher rates of hemodynamic compromise presentations with ST compared to *de novo* lesions which would underestimate the adverse prognosis of ST recorded by hospital-based registries.

In addition to the earlier presentation to hospital, patients in the ST group had comparable rates of successful revascularization to the *de novo* group (94.9% vs. 95.4%, p=0.79) with no significant differences in TIMI flow post-PCI (p=0.30) despite higher rates of TIMI flow grade 0 pre-PCI (83.9% vs. 60.3%, p<0.001) and complex lesion characteristics such as lesion type B2/C classification (79.6% vs. 69.5%, p=0.012) and bifurcation lesions (79.6% vs. 69.5%, p=0.012) in the ST group. In contrast to our study, Chechi *et al.* [5] reported lower rates of successful angiographic revascularization in patients presenting with STEMI secondary to ST compared to *de novo* lesions-related STEMIs, and also described ST as an independent predictor of unsuccessful reperfusion. However, IVUS use was not reported in that study, and the MACE rates were similar between the two groups at 6 months for in-hospital survivors. The use of IVUS in our cohort of patients presenting with STEMI was more frequent in ST group compared to the *de novo* group (6.6% vs. 0.2%, p<0.01). Additional information of lesion characteristics and stent expansion/apposition obtained from the use of IVUS may have played a role in the successful revascularization rates in our study. This has been demonstrated by other reports that described the benefits of IVUS utilization during PCI [18,19]. A study by Lim *et al.* [20] described worse outcomes with ACS secondary to ST compared to *de novo* lesions despite the equivalent use of IVUS in both groups. However, unlike our study, non-STEMI comprised about 38% of their study population. Moreover, a recent study reported an independent association of STBT with failure of angiographic revascularization in

acute ST [21]. Therefore, both the shorter STBT coupled with the higher use of IVUS in the ST group may have contributed to the comparable successful revascularization rates to the *de novo* group in our study.

Much of the ST in our study was comprised of VLST which is in accord with findings from other reports [4,22,23]. Mechanistic studies using optical coherence tomography identified malapposition, neoatherosclerosis, stent underexpansion and uncovered struts as common findings in patients with VLS T[24,25]. Kubo *et al*. [26] described better outcomes with VLST compared to EST and LST. Likewise, Kukreja *et al*. [27] also reported higher mortality rates in patients with ACS secondary to EST, whereas VLST and LST had no apparent increase in mortality. Equivalent long-term outcomes of STEMI-related VLST compared to *de novo* lesions causing STEMI were also reported by Viveiros Monteira *et al* [14]. The lack of independent association between LST and VLST and worse outcomes on multivariate analysis in our study corroborate these findings. A possible explanation for the poorer outcomes with EST compared to LST and VLST is the vulnerability of the myocardium in the early recovery period following PCI to acute insults such as EST, particularly that the majority of ST occur in patients with previous ACS or history of MI [4,27]. Additionally, the remote ischemic event caused by VLST in a myocardium that had survived previous MI may not impart an adverse prognostic effect of similar magnitude to an ischemic event occurring in an intact myocardium, such as the case of patients in the *de novo* group.

In our STEMI cohort, the rates of no-reflow phenomenon complicating PCI were similar between the ST group and the *de novo* group which is in accord with other studies [13,26]. The no-reflow phenomenon has been shown to independently predict adverse short- and long-term clinical outcomes in the setting of PCI [28,29]. In contrast to those findings, a study by Lim *et al.* demonstrated higher rates of this phenomenon in ST as well as an increased mortality

in patients with ST and described the no-reflow phenomenon as an independent predictor of ST [20]. The similar rates of no reflow complicating PCI in the ST and the *de novo* groups in our study could partly explain the comparable prognosis in those two cohorts. In-hospital complications, particularly bleeding, were more frequent in the ST group with a greater requirement for blood transfusion compared to the *de novo* group ($p<0.05$). This complication is possibly related to the greater use of GP IIb/IIIa inhibitors that are used to treat thrombotic occlusions and are known to increase bleeding rates [30]. Dangas *et al.* performed a large-scale pooled analysis of 4,935 patients from two randomized clinical trials that assessed 30-day outcomes following PCI when randomized to either bivalirudin or heparin ± GP IIb/IIIa inhibitor [31]. The authors reported an increased frequency of early ST in the bivalirudin group, however, there was a lower mortality attributable to early-ST in the bivalirudin group than the heparin ± GP IIb/IIIa inhibitor group. The optimal use of heparin, GP IIb/IIIa inhibitors, bivalirudin or their combinations in the setting of ST and PCI remains controversial [32].

Our study had a number of limitations that need to be acknowledged. First, this was a retrospective analysis of patients enrolled prospectively in a PCI registry, which brings its own inherent limitations including an inability to account for unmeasured confounders. Second, the study may not have been powered to detect small differences between groups given the relatively small numbers in the ST group. Third, we only included patients who underwent PCI and therefore the results may not able to be extrapolated to patients with STEMI who undergo thrombolysis or receive conservative medical management only. Fourth, we did not report baseline medications used such as antiplatelet therapies as well as baseline laboratory values such as haemoglobin or platelet count. Finally, the reporting of stent thrombosis could have varied amongst cardiologists and core laboratory verification of angiograms was not performed in our study.

Conclusion

This study findings highlight the similar rates of short- and intermediate-term mortality amongst patients with STEMI secondary to ST compared to *de novo* lesions who underwent primary PCI. Overall, the rates of in-hospital mortality and MACE were equivalent between the two groups and ST was not independently associated with adverse outcomes at 30-days on multivariate analysis. Very-late stent thrombosis was the most common form of ST, and further measures are needed to prevent this morbid complication.

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Figure 1. Kaplan-Meier 30-day survival estimates for mortality and MACE comparing the ST group with the *de novo* group

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Table 1. Baseline demographic and clinical characteristics of patients with STEMI undergoing PCI from the MIG registry.

	ST group (n=128)	*De Novo* group (n=3,835)	P value
Age (years), mean ± SD	65.51 ± 11.23	62.68 ± 12.51	**0.011**
Women, n (%)	21 (16.4)	817 (21.3)	0.18
BMI kg/m2, mean ± SD	26.9 ± 4.2	27.9 ± 5.0	**0.01**
Diabetes, n (%)	30 (23.4)	620 (16.2)	**0.029**
Diabetic status, n (%)			*0.056*
Non-diabetic	98 (76.6)	3,211 (83.8)	
Non-insulin requiring	21 (16.4)	476 (12.4)	
Insulin requiring	9 (7.0)	144 (3.8)	
Hypertension, n (%)	99 (77.3)	1,997 (52.2)	**<0.001**
Dyslipidemia, n (%)	103 (80.5)	1,726 (45.1)	**<0.001**
Smoking status, n (%)			**0.001**
Current smoker	39 (30.7)	1,429 (38.4)	
Previous smoker	55 (43.3)	1,026 (27.6)	
Never smoker	33 (26)	1,269 (34.1)	
Renal function, n (%)			*0.076*
GFR >60 mL/min	81 (67.5)	2,453 (74.5)	
GFR 30-59 mL/min	33 (27.5)	765 (23.2)	
GFR <30 mL/min	6 (5.0)	76 (2.3)	
Dialysis, n (%)	1 (0.78)	14 (0.37)	0.45
Previous MI, n (%)	105 (82.0)	331 (8.6)	**<0.001**

Family history of CAD, n (%)	37 (31.4)	1,191 (33.0)	0.70
Heart failure, n (%)	5 (3.9)	46 (1.2)	**0.008**
Cerebrovascular disease, n (%)	9 (7.0)	152 (4.0)	*0.085*
Peripheral vascular disease, n (%)	10 (7.8)	98 (2.6)	**<0.001**
Atrial fibrillation, n (%)	4 (3.2)	242 (6.4)	0.148
Chronic lung disease, n (%)	13 (10.2)	320 (8.4)	0.47
Ejection fraction category, n (%)			0.231
LVEF >45%	68 (59.7)	2,435 (67.3)	
LVEF 30%-45%	43 (37.7)	1,114 (30.8)	
LVEF <30%	3 (2.6)	71 (2.0)	
Previous PCI, n (%)	128 (100%)	235 (6.1)	
Previous CABG, n (%)	9 (7.0)	69 (1.8)	**<0.001**
Previous valvular surgery, n (%)	1 (0.78)	16 (0.42)	0.53
Out-of-hospital cardiac arrest, n (%)	6 (4.7)	440 (11.5)	**0.017**
In-hospital pre-procedural arrest, n (%)	2 (4.9)	104 (6.0)	0.77
Pre-procedural intubation, n (%)	3 (7.3)	109 (6.2)	0.77
Procedural intubation, n (%)	1 (2.4)	51 (2.9)	0.857
Cardiogenic shock, n (%)	15 (11.7)	399 (10.4)	0.63
IABP, n (%)	10 (11.0)	185 (8.7)	0.439
Intravenous inotropes requirement, n (%)	15 (11.7)	401 (10.5)	0.654

BMI, body mass index; GFR, glomerular filtration rate; IABP, intra-aortic balloon pump; LVEF, left ventricular ejection fraction;

Table 2. Procedural findings and characteristics.

	ST group (n=128)	*De Novo* group (n=3,835)	P value
Multi-vessel disease, n (%)	77 (60.2)	1,980 (51.6)	*0.058*
Symptom-to-door time in minutes, median (IQR)	101.5 (71-162)	114 (75-210)	**0.032**
Door-to-balloon time <90 min, n (%)	75 (67.2)	2,703 (70.7)	0.388
Door-to-balloon time in minutes, median (IQR)	66 (43.5-97.5)	67 (44-96)	0.947
Symptom-to-balloon time in minutes, median (IQR)	184.5 (132-239)	194 (141-291)	0.*051*
Femoral access, n (%)	100 (78.1)	2,811 (73.3)	0.224
GP IIb/IIIa inhibitor use, n (%)	96 (75.0)	2,355 (61.4)	**0.002**
Unfractionated Heparin, n (%)	125 (97.7)	3,807 (99.3)	**0.041**
Bivalirudin, n (%)	3 (2.3)	29 (0.8)	**0.048**
Previous stent type in ST group, n (%)	62 (48.8)	-	-
DES	59 (46.5)	-	
BMS	5 (3.9)	-	
Mixed DES & BMS	1 (0.79)	-	
Temporal types of ST, n (%)			-
EST	23 (16.8)	-	
LST	26 (19)	-	

VLST	77 (64.2)	-	
Number of days to stent thrombosis, median (IQR)	1187 [119 – 2491]	-	-
Culprit lesion in LAD, n (%)	64 (46.7)	1,613 (36.3)	**0.013**
Culprit lesion in proximal LAD, n (%)	32 (23.4)	852 (19.2)	0.22
Culprit in RCA, n (%)	42 (30.7)	1,762 (39.7)	**0.033**
Culprit in LCx, n (%)	13 (9.5)	429 (9.7)	0.94
Culprit in left main coronary artery, n (%)	3 (2.2)	35 (0.8)	*0.075*
Bypass graft culprit lesion, n (%)	5 (3.7)	30 (0.7)	**<0.001**
Complex lesion (Type B2/C), n (%)	109 (79.6)	3,087 (69.5)	**0.012**
Ostial location of the culprit lesion, n (%)	12 (8.8)	332 (7.5)	0.57
Bifurcation location of the culprit lesion, n (%)	22 (16.1)	475 (10.7)	**0.047**
Pre-stenosis, mean ± SD	97.67 ± 8.96	94.82 ± 10.91	**<0.001**
Post-stenosis, mean ± SD	5.43 ± 17.21	4.90 ± 19.42	**0.002**
TIMI flow pre-PCI, n (%)			**<0.001**
0	115 (83.9)	2,676 (60.3)	
1	6 (4.4)	243 (5.5)	
2	5 (3.7)	479 (10.8)	
3	11 (8.0)	1,037 (23.4)	
TIMI flow post-PCI, n (%)			0.30

0	2 (1.5)	122 (2.7)	
1	3 (2.2)	38 (0.9)	
2	3(2.2)	124 (2.8)	
3	129 (94.1)	4,155 (93.6)	
Successful revascularization, n (%)	130 (94.9)	4,235 (95.4)	0.79
IVUS, n (%)	9 (6.6)	8 (0.2)	**<0.001**
Balloon, n (%)	61 (44.5)	306 (6.9)	**<0.001**
Stent type used, n (%)			**<0.001**
DES	63 (40.6)	1,805 (47.0)	
BMS	21 (16.4)	1,815 (47.3)	
Mean stent length, mean ± SD	20.0 ± 7.6	19.2 ± 6.1	0.74
Total stent length, mean ± SD	22.7 ± 11.0	21.7 ± 9.7	0.66
Mean stent diameter, mean ± SD	2.99 ± 0.45	3.04 ± 0.51	0.54
Acute closure, n (%)	2 (1.5)	30 (0.7)	0.27
Dissection, n (%)	3 (2.2)	163 (3.7)	0.36
Perforation, n (%)	0	15 (0.3)	0.49
No-reflow phenomenon, n (%)			0.9
Transient	4 (2.9)	162 (3.7)	
Persistent	2 (1.5)	61 (1.4)	

BMS, bare-metal stent; DES, drug-eluting stent; GP IIb/IIIa, Glycoprotein IIb/IIIa; IVUS, intra-vascular ultrasound; LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

Table 3. Medication use at 30 days.

	ST group (n= 128)	*De Novo* group (n=3,835)	P value
Aspirin, n (%)	112 (99.1)	3,364 (97.5)	0.27
Other antiplatelet agents, n (%)	108 (95.6)	3,333 (96.6)	0.57
Warfarin/NOAC, n (%)	12 (10.8)	360 (10.5)	0.90
ACE-I/ARB, n (%)	94 (84.7)	3,044 (88.3)	0.24
Beta Blockers, n (%)	97 (87.4)	3,095 (98.9)	0.39
Statin, n (%)	107 (96.4)	3,336 (97.2)	0.62

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; NOAC, new oral anticoagulant.

Table 4. Short- and intermediate-term outcomes in both groups.

	ST group (n= 128)	*De Novo* group (n=3,835)	P value
In-hospital outcomes			
Emergency PCI, n (%)	1 (0.8)	31 (0.8)	0.97
Unplanned CABG, n (%)	3 (2.3)	69 (1.8)	0.65
Arrhythmia, n (%)	26 (20.3)	738 (19.2)	0.76
Stroke, n (%)	1 (0.8)	32 (0.8)	0.94
Congestive heart failure, n (%)	14 (10.9)	344 (9)	0.44
Renal impairment, n (%)	5 (3.9)	143 (3.7)	0.91
Bleeding, n (%)	11 (8.6)	171 (4.5)	**0.028**
Bleeding site, n (%)			0.80
Percutaneous entry	2 (18.2)	24 (14.8)	
Retroperitoneal	0	7 (4.3)	
Other	9 (81.8)	131 (80.9)	
Blood transfusion, n (%)	8 (16)	107 (5.7)	**0.002**
Access site occlusion, n (%)	0	1 (0.03)	0.85
Loss of distal pulse, n (%)	1 (0.8)	1 (0.03)	**<0.001**
Dissection, n (%)	0	8 (0.2)	0.60
Arteriovenous fistula, n (%)	0	2 (0.05)	0.79
Pseudoaneurysm, n (%)	1 (0.8)	17 (0.4)	0.57
In-hospital mortality, n (%)	6 (4.7)	250 (6.5)	0.40
Cardiac related mortality, n (%)	5 (83.3)	209 (83.6)	0.98
Length of stay, mean ± SD	5.03 ± 3.40	5.42 ± 6.11	0.32

30-day outcomes			
Mortality, n (%)	6 (4.7)	271 (7.1)	0.29
Cardiac related mortality, n (%)	5 (83.3)	219 (80.8)	0.87
TLR, n (%)	6 (4.7)	111 (2.9)	0.23
TVR, n (%)	7 (5.5)	126 (3.3)	0.17
Stroke, n (%)	1 (0.8)	35 (0.9)	0.87
Readmission, n (%)	9 (7.5)	461 (13)	*0.077*
MACE, n (%)	13 (10.2)	408 (10.6)	0.86
MACCE, n (%)	14 (10.9)	433 (11.3)	0.90

major adverse cardiac and cerebral events; MACE, major adverse cardiac events; MACCE;

TLR, target lesion revascularization; TVR, target vessel revascularization;

Table 5. Multivariate predictors of 30-day mortality and MACE in both groups.

	Odds Ratio of 30-day Mortality	95% Confidence Interval	p Value	Odds Ratio of 30-day MACE	95% Confidence Interval	p Value
Ejection fraction <30%	9.8	4.5 – 21.1	<0.001	7.3	3.9 – 13.8	<0.001
Previous valve surgery	8.3	1.6 – 40.9	0.009	NA	NA	NA
Glomerular filtration rate <30 ml/min/1.73m^2	8.1	3.8 – 17.3	<0.001	3.5	1.8 – 6.6	<0.001
Out-of-hospital cardiac arrest	7.9	5 – 12.5	<0.001	3.8	2.6 – 5.4	<0.001
Cardiogenic shock	4.7	3 – 7.2	<0.001	3.3	2.3 – 4.8	<0.001
Ejection Fraction 45% - 30%	3.3	2.1 – 5.2	<0.001	2.1	1.6 – 2.8	<0.001
No-reflow phenomenon	2.8	1.1 – 7.5	0.03	2.5	1.1 – 5.6	0.02
Chronic lung disease	2.1	1.2 – 3.6	0.005	2.2	1.5 – 3.2	<0.001
Glomerular filtration rate 30 – 59 ml/min/1.73m^2	2	1.3 – 3	<0.001	1.4	1.1 – 1.9	<0.001
Age (per year)	1	1.03 – 1.07	0.001	1.02	1.01 – 1.03	<0.001
Right coronary artery culprit	0.4	0.2 – 0.7	<0.001	NA	NA	NA
Left main coronary artery disease	5.4	1.7 – 17.2	0.004	4.1	1.4 – 12.1	0.01

Drug-eluting stent use	0.04	0.2 – 0.6	<0.001	0.4	0.28 – 0.51	<0.001
Diabetes	NA	NA	NA	1.7	1.2 – 2.3	<0.01
Stent thrombosis	0.28	0.07 – 1.09	0.068	0.88	0.42 – 1.9	0.75

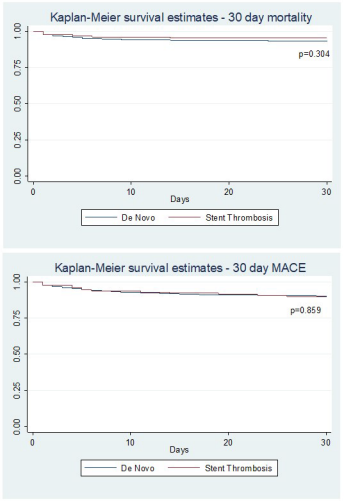

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Table 2. Procedural findings and characteristics.

	ST group (n=128)	*De Novo* group (n=3,835)	P value
Multi-vessel disease, n (%)	77 (60.2)	1,980 (51.6)	*0.058*
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Door-to-balloon time <90 min, n (%)	75 (67.2)	2,703 (70.7)	0.388
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Bivalirudin, n (%)	3 (2.3)	29 (0.8)	**0.048**
Previous stent type in ST group, n (%)	62 (48.8)	-	-
DES	59 (46.5)	-	
BMS	5 (3.9)	-	
Mixed DES & BMS	1 (0.79)	-	
Temporal types of ST, n (%)			-
EST	23 (16.8)	-	
LST	26 (19)	-	
VLST	77 (64.2)	-	

Number of days to stent thrombosis, median (IQR)	1187 [119 – 2491]	-	-
Culprit lesion in LAD, n (%)	64 (46.7)	1,613 (36.3)	**0.013**
Culprit lesion in proximal LAD, n (%)	32 (23.4)	852 (19.2)	0.22
Culprit in RCA, n (%)	42 (30.7)	1,762 (39.7)	**0.033**
Culprit in LCx, n (%)	13 (9.5)	429 (9.7)	0.94
Culprit in left main coronary artery, n (%)	3 (2.2)	35 (0.8)	*0.075*
Bypass graft culprit lesion, n (%)	5 (3.7)	30 (0.7)	**<0.001**
Complex lesion (Type B2/C), n (%)	109 (79.6)	3,087 (69.5)	**0.012**
Ostial location of the culprit lesion, n (%)	12 (8.8)	332 (7.5)	0.57
Bifurcation location of the culprit lesion, n (%)	22 (16.1)	475 (10.7)	**0.047**
Pre-stenosis, mean ± SD	97.67 ± 8.96	94.82 ± 10.91	**<0.001**
Post-stenosis, mean ± SD	5.43 ± 17.21	4.90 ± 19.42	**0.002**
TIMI flow pre-PCI, n (%)			**<0.001**
0	115 (83.9)	2,676 (60.3)	
1	6 (4.4)	243 (5.5)	
2	5 (3.7)	479 (10.8)	
3	11 (8.0)	1,037 (23.4)	
TIMI flow post-PCI, n (%)			0.30
0	2 (1.5)	122 (2.7)	
1	3 (2.2)	38 (0.9)	

2	3(2.2)	124 (2.8)	
3	129 (94.1)	4,155 (93.6)	
Successful revascularization, n (%)	130 (94.9)	4,235 (95.4)	0.79
IVUS, n (%)	9 (6.6)	8 (0.2)	**<0.001**
Balloon, n (%)	61 (44.5)	306 (6.9)	**<0.001**
Stent type used, n (%)			**<0.001**
DES	63 (40.6)	1,805 (47.0)	
BMS	21 (16.4)	1,815 (47.3)	
Mean stent length, mean ± SD	20.0 ± 7.6	19.2 ± 6.1	0.74
Total stent length, mean ± SD	22.7 ± 11.0	21.7 ± 9.7	0.66
Mean stent diameter, mean ± SD	2.99 ± 0.45	3.04 ± 0.51	0.54
Acute closure, n (%)	2 (1.5)	30 (0.7)	0.27
Dissection, n (%)	3 (2.2)	163 (3.7)	0.36
Perforation, n (%)	0	15 (0.3)	0.49
No-reflow phenomenon, n (%)			0.9
Transient	4 (2.9)	162 (3.7)	
Persistent	2 (1.5)	61 (1.4)	

BMS, bare-metal stent; DES, drug-eluting stent; GP IIb/IIIa, Glycoprotein IIb/IIIa; IVUS, intra-vascular ultrasound; LAD, left anterior descending; LCx, left circumflex; RCA, right coronary artery; TIMI, thrombolysis in myocardial infarction.

Table 3. Medication use at 30 days.

	ST group (n= 128)	*De Novo* group (n=3,835)	P value
Aspirin, n (%)	112 (99.1)	3,364 (97.5)	0.27
Other antiplatelet agents, n (%)	108 (95.6)	3,333 (96.6)	0.57
Warfarin/NOAC, n (%)	12 (10.8)	360 (10.5)	0.90
ACE-I/ARB, n (%)	94 (84.7)	3,044 (88.3)	0.24
Beta Blockers, n (%)	97 (87.4)	3,095 (98.9)	0.39
Statin, n (%)	107 (96.4)	3,336 (97.2)	0.62

ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; NOAC, new oral anticoagulant.

Table 4. Short- and intermediate-term outcomes in both groups.

	ST group (n= 128)	*De Novo* group (n=3,835)	P value
In-hospital outcomes			
Emergency PCI, n (%)	1 (0.8)	31 (0.8)	0.97
Unplanned CABG, n (%)	3 (2.3)	69 (1.8)	0.65
Arrhythmia, n (%)	26 (20.3)	738 (19.2)	0.76
Stroke, n (%)	1 (0.8)	32 (0.8)	0.94
Congestive heart failure, n (%)	14 (10.9)	344 (9)	0.44
Renal impairment, n (%)	5 (3.9)	143 (3.7)	0.91
Bleeding, n (%)	11 (8.6)	171 (4.5)	**0.028**
Bleeding site, n (%)			0.80
Percutaneous entry	2 (18.2)	24 (14.8)	
Retroperitoneal	0	7 (4.3)	
Other	9 (81.8)	131 (80.9)	
Blood transfusion, n (%)	8 (16)	107 (5.7)	**0.002**
Access site occlusion, n (%)	0	1 (0.03)	0.85
Loss of distal pulse, n (%)	1 (0.8)	1 (0.03)	**<0.001**
Dissection, n (%)	0	8 (0.2)	0.60
Arteriovenous fistula, n (%)	0	2 (0.05)	0.79
Pseudoaneurysm, n (%)	1 (0.8)	17 (0.4)	0.57
In-hospital mortality, n (%)	6 (4.7)	250 (6.5)	0.40
Cardiac related mortality, n (%)	5 (83.3)	209 (83.6)	0.98
Length of stay, mean ± SD	5.03 ± 3.40	5.42 ± 6.11	0.32
30-day outcomes			

Mortality, n (%)	6 (4.7)	271 (7.1)	0.29
Cardiac related mortality, n (%)	5 (83.3)	219 (80.8)	0.87
TLR, n (%)	6 (4.7)	111 (2.9)	0.23
TVR, n (%)	7 (5.5)	126 (3.3)	0.17
Stroke, n (%)	1 (0.8)	35 (0.9)	0.87
Readmission, n (%)	9 (7.5)	461 (13)	*0.077*
MACE, n (%)	13 (10.2)	408 (10.6)	0.86
MACCE, n (%)	14 (10.9)	433 (11.3)	0.90

major adverse cardiac and cerebral events; MACE, major adverse cardiac events; MACCE; TLR, target lesion revascularization; TVR, target vessel revascularization;

Table 5. Multivariate predictors of 30-day mortality and MACE in both groups.

	Odds Ratio of 30-day Mortality	95% Confidence Interval	p Value	Odds Ratio of 30-day MACE	95% Confidence Interval	p Value
Ejection fraction <30%	9.8	4.5 – 21.1	<0.001	7.3	3.9 – 13.8	<0.001
Previous valve surgery	8.3	1.6 – 40.9	0.009	NA	NA	NA
Glomerular filtration rate <30 ml/min/1.73m^2	8.1	3.8 – 17.3	<0.001	3.5	1.8 – 6.6	<0.001
Out-of-hospital cardiac arrest	7.9	5 – 12.5	<0.001	3.8	2.6 – 5.4	<0.001
Cardiogenic shock	4.7	3 – 7.2	<0.001	3.3	2.3 – 4.8	<0.001
Ejection Fraction 45% - 30%	3.3	2.1 – 5.2	<0.001	2.1	1.6 – 2.8	<0.001
No-reflow phenomenon	2.8	1.1 – 7.5	0.03	2.5	1.1 – 5.6	0.02
Chronic lung disease	2.1	1.2 – 3.6	0.005	2.2	1.5 – 3.2	<0.001
Glomerular filtration rate 30 – 59 ml/min/1.73m^2	2	1.3 – 3	<0.001	1.4	1.1 – 1.9	<0.001
Age (per year)	1	1.03 – 1.07	0.001	1.02	1.01 – 1.03	<0.001
Right coronary artery culprit	0.4	0.2 – 0.7	<0.001	NA	NA	NA
Left main coronary artery disease	5.4	1.7 – 17.2	0.004	4.1	1.4 – 12.1	0.01
Drug-eluting stent use	0.04	0.2 – 0.6	<0.001	0.4	0.28 – 0.51	<0.001

Diabetes	NA	NA	NA	1.7	1.2 – 2.3	<0.01
Stent thrombosis	0.28	0.07 – 1.09	0.068	0.88	0.42 – 1.9	0.75